

pending on the size of the pregnancy, the patient's desire for future fertility, and the ability to control hemostasis. Laparoscopic therapy will generally require a primary infraumbilical incision for the laparoscope and two or more smaller incisions in the suprapubic region for ancillary trocars. The outcome of subsequent pregnancies for women treated laparoscopically for the ectopic pregnancies is similar to that achieved by traditional exploratory laparotomy. There is a persistence rate of about 5% with laparoscopic salpingostomy, so these patients must be observed postoperatively with serial β -HCG measurements.

Medical therapy with methotrexate may be used first or to treat patients with persistently elevated β -HCG values after laparoscopic salpingostomy. One regimen is to give methotrexate, 1.0 mg per kg, and leucovorin calcium (citrovorum factor), 0.1 mg per kg, on alternating days until the β -HCG values decrease by 15% on two consecutive days. A maximum of four doses can be used consecutively. Criteria for medical therapy include hemodynamic stability, the absence of hepatic or renal disease, certain diagnosis (when a nonviable intrauterine pregnancy has been ruled out), and an adnexal mass measuring less than 3.5 cm sonographically in its greatest dimension. These patients should be counseled and observed closely with β -HCG values and liver function tests because about 4% will have tubal rupture and require surgical management. Results as measured by the patency of fallopian tubes by hysterosalpingogram and by subsequent pregnancy seem to compare favorably with surgical management.

Laparoscopic therapy and medical therapy for ectopic pregnancy are important advances because of their favorable patient acceptance and the potential effect on the economics of health care.

VERA A. TORP, MD
San Diego, California

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Genetic Predisposition to Ovarian Cancer

OVARIAN CANCER remains the most common cause of death from gynecologic malignancy in developed countries. It was estimated that in 1991 20,700 new cases and about 13,000 deaths would occur in the United States alone. The "lifetime risk" of ovarian cancer developing in a woman in the United States is about 1.4%, with the vast majority of tumors (85% to 90%) being epithelial in origin.

Although the cause of ovarian carcinoma remains unclear, genetic susceptibility is an important risk factor. Pedigree analysis has revealed three distinct patterns of familial transmission involving epithelial ovarian cancer. The most common syndrome is site-specific, and the heritable risk is limited to cancer of the ovary. The second is often referred to as the breast-ovarian carcinoma syndrome, and women in these families are at increased risk for one or both cancers developing. The cancer family syndrome also involves ovarian cancer in association with endometrial, breast, and colon carcinomas.

The pattern of transmission for each is autosomal dominant with variable penetrance. Women with two or more first-degree relatives with ovarian carcinoma have as much as a 50% risk of becoming affected. An important factor is that

in the first two syndromes, men may be carriers of the gene and can transmit it to half of their offspring. In the cancer family syndrome (Lynch syndrome II), men are also at risk for adenocarcinomas, especially colorectal, and transmit the deleterious gene to half of their daughters and sons. It is currently impossible to quantitate the risk in a woman with one first-degree relative or second-degree relatives who have ovarian cancer, although it is safe to say that it is greater than that in the population as a whole. Careful surveillance should begin in women in their early 20s.

The genetics of ovarian carcinoma have not been well described. A loss of alleles on chromosomes 1, 3, 6, 11, and 17 has been detected, which may represent the deletion of tumor-suppressor genes. The amplification of several proto-oncogenes has also been described.

Many physicians advise prophylactic oophorectomy for women at risk for familial ovarian cancer. The age of onset is significantly lower in patients with hereditary ovarian carcinoma, and, this being the case, oophorectomy is often done as soon as childbearing is completed. It has been recommended that routine pelvic examinations be expanded to include annual pelvic ultrasonography and the assessment of serum CA 125 levels starting at age 25 for women in this high-risk group. Unfortunately, oophorectomy does not offer complete protection. Adenocarcinoma of the mesothelium, which is histologically indistinguishable from ovarian cancer, has occurred in several patients.

Genetic risk factors account for only a small proportion of all patients with cancer of the ovaries, with estimates as high as 10% but more likely 3% to 5%. Still, this group represents a population that is important in terms of surveillance, prevention, and as an opportunity to further our understanding of this disease.

JAMES L. FREDDO, MD
San Diego, California

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Ovarian Cancer Screening

SCREENING FOR ovarian cancer has begun to receive a great deal of publicity both within the areas of clinical research and in the news media. This is undoubtedly due in part to the tragic and well-publicized deaths of young women with advanced disease; it is also likely caused by the frustration of dealing with a cancer that will strike more than 20,000 women annually, leaving about 13,000 dead. Because these cancers are detected in later stages, those afflicted have only a 13% to 20% chance of surviving five years. The early detection of other cancers has increased survival. Recommendations for ovarian cancer screening are aimed at detecting ovarian cancer at earlier stages in hopes of prolonging survival.

Tools now widely available for screening include the biochemical marker, CA 125, and ultrasonography. CA 125 represents an antigen to the coelomic epithelial derivatives and is measured in the serum using a monoclonal antibody. Its greatest use thus far is in the management of ovarian cancer patients with respect to regression or progression of

known disease. Unfortunately, elevated CA 125 levels are also seen in early pregnancy, endometriosis, pancreatitis, peritonitis, ascites, menstruation, fibroids, and pelvic inflammatory disease among other benign conditions, which limits its usefulness in screening for early ovarian cancers.

Ultrasonographers have developed strict criteria for describing pelvic masses likely to be malignant. Such sonographic criteria include ovarian echogenicity, an irregular contour, and a volume greater than 20 ml. They admit that these sonographic criteria cannot distinguish between early malignant and benign conditions. False-positive studies can lead to unnecessary or inappropriate surgical procedures with their attendant morbidity or even mortality. Even in combination with an abnormal CA 125 serum study and abnormal findings on a pelvic examination, the detection rate of ovarian malignancy with ultrasonography is not 100%.

A new diagnostic technique, transvaginal color Doppler ultrasonography, has shown some promise in identifying dynamic characteristics of normal versus neoplastic ovaries. Color Doppler quantifies the flow in these low-resistance vessels using a calculated "resistance index." A resistance index of less than 0.40 is considered abnormal. More studies

are needed to determine the effectiveness of this technique alone or in combination with other diagnostic methods.

Ultimately the cost-effectiveness of ovarian cancer screening will need to address the number of surgical procedures that will be done to confirm the diagnosis. For the time being, no single test or combination of tests has been shown to be an effective predictor of early stage disease. Except for the high-risk population of women with first-degree relatives with a confirmed diagnosis of ovarian cancer, there appears to be no suitable test or combination of tests to warrant the routine screening of healthy, asymptomatic women for ovarian cancer.

CYNTHIA I. MACRI, MD
PHILIP J. DiSAIA, MD
Orange, California

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